This listing will replace all prior versions and listings of claims in the application. The claims are marked in the manner provided in the announcement dated January 13, 2003 from Stephen Kunin, Deputy Commissioner for Patent Examination Policy, entitled "Amendment in a Revised Format is now Permitted," which is posted on the USPTO information web pages.

Listing of Claims:

Claim 1. (currently amended) A method of establishing a patient-specific optimally effective therapeutic dose for administration of a radiopharmaceutical to a patient, the method comprising:

determining a maximum tolerated dose for the radiopharmaceutical;

determining a desired total body dose of the radiopharmaceutical for the patient;

administering to the patient a trace dose of a radiopharmaceutical or an analog of the radiopharmaceutical;

determining a clearance profile for the radiopharmaceutical or a the radiopharmaceutical analog;

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determining the patient's mass and maximum effective mass;

selecting the lower of the patient's mass and maximum effective mass;

determining activity hours for the radiopharmaceutical or radiopharmaceutical analog based on the lower of the patient's mass or maximum effective mass and the desired total body dose;

determining residence time of an administered tracer dose of the radiopharmaceutical or the radiopharmaceutical analog in the whole body of the patient, the residence time being correlated to the clearance profile; and

establishing the optimally effective dose of the radiopharmaceutical for the patient by solving for therapeutic dose in the following equation:

$$\text{therapeutic dose} = \frac{\text{Activity Hours}}{\text{Residence time}} \times \frac{\text{desired total body dose}}{\text{maximum tolerated dose.}}$$

Claim 2. (original) The method of claim 1, wherein the step of determining the maximum tolerated dose comprises performing a dose escalation study for the radiopharmaceutical in a patient population.

Claim 3. (cancelled)

Claim 4. (previously amended) The method of claim 1, wherein the maximum effective mass is correlated to lean body mass of the patient.

Claim 5. (original) The method of claim 1, wherein the maximum effective mass is based on the gender and height of the patient.

Claim 6. (original) The method of claim 1, wherein the step of determining the clearance profile comprises performing a study following measurement over time of the loss of radioactivity from an administered radiopharmaceutical.

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Claim 7. (original) The method of claim 1, wherein the step of determining the clearance profile comprises performing a dose escalation study for the radiopharmaceutical.

Claim 8. (original) The method of claim 1, wherein the clearance profile provides an activity-time curve shape for the radiopharmaceutical.

Claim 9. (original) The method of claim 1, wherein the clearance profile provides an indication of the number of exponential terms in the function defining the pattern of clearance for the radiopharmaceutical.

Claim 10. (original) The method of claim 1, wherein the step of determining the residence time for the radiopharmaceutical comprises:

making measurements of radioactivity in the whole body of the patient at each of a number of time points,

calculating percent injected activity of the radiopharmaceutical at each of the time points, and

establishing the residence time by plotting the time points vs. percent injected activity on a semilog graph and determining 37% injected activity.

Claim 11. (original) The method of claim 10, wherein each time point is background corrected.

Claim 12. (original) The method of claim 10, wherein the number of time points are correlated to the clearance profile of the radiopharmaceutical so that at least 2 measurements are made if the radiopharmaceutical has monoexponential clearance, at least 4 measurements are made if the radiopharmaceutical has biexponential clearance, and at least 6 measurements are made if the radiopharmaceutical has triexponential clearance.

Claim 13. (original) The method of claim 1, wherein the step of determining the residence time for the radiopharmaceutical comprises:

making measurements of radioactivity in the whole body of the patient at each of three time points and solving in the following equation:

$$\text{Residence time (hr)} = \frac{t_2\,(1-\frac{C_2}{C_1})}{\log_e\,(\frac{C_1}{C_2})} + \frac{\frac{C_2}{C_1}(t_3-t_2)}{\log_e\,(\frac{C_2}{C_3})}$$

where t_1, t_2, and t_3 are the three time points and c_1, c_2, and c_3 are the counts at each of the t_1, t_2, and t_3 time points.

Claim 14. (original) The method of claim 13, wherein each time point is background corrected.

Claim 15. (original) The method of claim 1, wherein the step of determining the residence time for the radiopharmaceutical comprises:

making measurements of radioactivity in the whole body of the patient at each of a number of time points, and solving for τ in the following equation:

$$\tau = \frac{\sum_{i=1}^{n} \frac{a_i}{\alpha_i}}{\sum_{i=1}^{n} a_i}$$

where τ is residence time, n is the number of exponential terms as determined by the clearance profile, a_i are the intercepts, and α_i are the slopes of the *i*th exponential term.

Claim 16. (original) The method of claim 15, wherein each time point is background corrected.

Claim 17. (original) The method of claim 15, wherein the number of time points are correlated to the clearance profile of the radiopharmaceutical so that at least 2 measurements are made if the radiopharmaceutical has monoexponential clearance, at least 4 measurements are made if the radiopharmaceutical has biexponential clearance, and at least 6 measurements are made if the radiopharmaceutical has triexponential clearance.

Claim 18. (previously amended) The method of claim 1, wherein the step of determining the residence time for the radiopharmaceutical comprises:

making measurements of radioactivity in the whole body of the patient at each of a number of time points, generating an activity-time curve, and using the trapezoidal rule or Simpson's rule to determine the residence time.

Claim 19. (currently amended) An optimally effective patient-specific therapeutic dose of a radiopharmaceutical for administration to a patient, said optimally effective therapeutic dose determined by the method comprising:

determining a maximum tolerated dose for the radiopharmaceutical;

determining a desired total body dose of the radiopharmaceutical for the patient;

<u>administering to the patient a trace dose of a radiopharmaceutical or an analog of the radiopharmaceutical;</u>

determining a clearance profile for the radiopharmaceutical or a <u>the</u> radiopharmaceutical analog;

determining the patient's mass and maximum effective mass;

selecting the lower of the patient's mass and maximum effective mass;

determining activity hours for the radiopharmaceutical or radiopharmaceutical analog based on the lower of the patient's mass or maximum effective mass and the desired total body dose;

determining residence time of an administered tracer dose of the radiopharmaceutical or the radiopharmaceutical analog in the whole body of the patient, the residence time being correlated to the clearance profile; and

establishing the optimally effective patient-specific dose of the radiopharmaceutical for the patient by solving for therapeutic dose in the following equation:

$$\text{therapeutic dose} = \frac{\text{Activity Hours}}{\text{Residence time}} \times \frac{\text{desired total body dose}}{\text{maximum tolerated dose.}}$$

Claim 20. (previously amended) A method of establishing a patient-specific optimally effective dose for administration of a radiopharmaceutical to a patient, the method comprising:

determining a clearance profile for the radiopharmaceutical or a radiopharmaceutical analog, said clearance profile providing a minimum number of time points for determination of the patient-specific residence time of the radiopharmaceutical or the radiopharmaceutical analog,

determining the desired total body dose (TBD) of the radiopharmaceutical for the patient;

determining the patient's mass (M) and maximum effective mass (MEM);

selecting the lower of the patient's mass and maximum effective mass (M or MEM);

determining activity hours (AH) for the radiopharmaceutical or a radiopharmaceutical analog by reference to Equation I:

$$AH = \frac{TBD \times (M \text{ or } MEM)}{\left[\sum_{elec} \Delta_{elect} + \sum_{phot} \Delta_{phot}\, \phi^{TB}_{phot}\right]}$$

(Equation I)

where $\left[\sum_{elec} \Delta_{elect} + \sum_{phot} \Delta_{phot}\, \phi^{TB}_{phot}\right]$

in Equation I represents the sum of electron energy and photon energy deposited in the total body of the patient by the radiopharmaceutical or radiopharmaceutical analog;

determining the patient-specific residence time of an administered tracer dose of the radiopharmaceutical or the radiopharmaceutical analog in the whole body of the patient; and

establishing a therapeutic dose of the radiopharmaceutical for the patient by dividing the activity hours by the patient-specific residence time to obtain a value and optionally multiplying the value by an attenuation factor, said attenuation factor being determined by the TBD divided by the maximum tolerated dose for the radiopharmaceutical.

Claim 21. (cancelled)

Claim 22. (original) The method of claim 20, wherein the step of determining the residence time for the radiopharmaceutical comprises:

making measurements of radioactivity in the whole body of the patient at each of a number of time points, and solving for τ in the following equation:

$$\tau = \frac{\sum_{i=1}^{n} \frac{a_i}{\alpha_i}}{\sum_{i=1}^{n} a_i}$$

where τ is residence time, n is the number of exponential terms as determined by the clearance profile, a_i are the intercepts, and α_i are the slopes of the *i*th exponential term.

Claim 23. (original) The method of claim 22, wherein each time point is background corrected.

Claim 24. (original) The method of claim 22, wherein the number of time points are correlated to the clearance profile of the radiopharmaceutical so that at least 2 measurements are made if the radiopharmaceutical has monoexponential clearance, at least 4 measurements are made if the

radiopharmaceutical has biexponential clearance, and at least 6 measurements are made if the radiopharmaceutical has triexponential clearance.

Claims 25-82 (cancelled)

Claim 83. (previously added) The method of claim 1 wherein the radiopharmaceutical is an ^{131}I-labeled anti-B1 antibody.

Claim 84. (previously amended) The optimally effective patient-specific therapeutic dose of claim 19 wherein the radiopharmaceutical is an ^{131}I-labeled anti-B1 antibody.

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Note: claims 13-18 and 22-14 were withdrawn by applicant during earlier prosecution but were considered by the Examiner (and rejected) in later Office Actions, including the latest Office Action of June 7, 2002. Accordingly, these claims are listed as pending rather than withdrawn.